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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,582	05/11/2005	Daniel Dube	MC073YP	3396

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EXAMINER	
RAHMANI, NILOOFAR	
ART UNIT	**PAPER NUMBER**
1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,582	DUBE ET AL.	
	Examiner	Art Unit	
	Niloofar Rahmani	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,11-18,20-22,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,11-18,20-22,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2, 11-18, 20-22, 25-26 are pending and claims 1, 3-10, 19, 23-24, and 27-34 are cancelled.

2. ***Priority***

This application is filed on 05/11/2005, which is a 371 of PCT/CA03/01800, filed on 11/19/2003, which claims benefit of 60/428,611, filed on 11/22/2002.

3. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the

inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims.
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn a method of treatment or prevention of asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), eosinophilic granuloma, psoriasis, inflammatory arthritis, osteoporosis,etc. using the compound of claim 2.

The state of the prior art: "Tumor necrosis factor (TNF) α is involved in the pathogenesis of established lymphoproliferative disease. Serum levels of TNFα and its soluble receptors are above normal values in B-cell chronic lymphocycle leukaemia (B-CLL) and they are valuable prognostic markers in lymphoma patients. Altered synthesis of TNFα has been associated with polymorphisms at the TNF gene cluster (i.e. TNFA, TNFB and LTB). The present study does not support the involvement of high TNFα and TNFβ –producing genotypes in a genetic predisposition to developing B-CLL. However, TNF polymorphic haplotypes in B-CLL may affect the patient's performance, outcome and disease

progression." (Mainou-Fowler et al., Leukemia and Lymphoma, 2000, Vol. 38, page 547-552).

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 2 would be useful for treating a pharmacological condition in a subject.

Amount of guidance/working examples: On pages 25-29 of the specification, applicant has examples of tested compounds and TNFα and LTB4 assays in human whole blood. However, applicant has no guidance or examples for treating any diseases using the compounds of formula (I) in claim 2.

The breadth of the claims: The breadth of claims is drawn to drawn a method of treatment or prevention of asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), eosinophilic granuloma, psoriasis, inflammatory arthritis, osteoporosis,etc. using the compound of claim 2.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), eosinophilic granuloma, psoriasis, inflammatory arthritis, osteoporosis,etc., one of ordinary

skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 25-26, for treating asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), eosinophilic granuloma, psoriasis, inflammatory arthritis, osteoporosis,etc., have been enabled by the instant specification.

4. Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that

would guide the skilled clinician to identify those who have the potential of becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning lines 14-33, page 16 to lines, page 1-2 lists the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted with diseases before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized to treat diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of inflammatory diseases generally. Under such circumstances, it is proper for the

PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent inflammatory diseases generally. That is, the skill is so low that no compound effective generally against inflammatory diseases has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "prevention".

5. *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S.

1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 11-18, 20-22, and 25-26 are rejected under 103(a) as being unpatentable over Li et al. of US 2003/0096829.

Determination of the scope and content of the prior art (MPEP §2141.01)

Li et al. disclosed a compound of formula (I) in claim 1, page 53 useful for treatment of asthma and inflammation.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims compounds and the prior art compounds is that the compounds of the instant claims has Y as a substituent in Ar being –COOH or $-C_{1-6}alkyl(C_{1-4}alkyl)_n$-COOH, wherein in the prior art the substituent in Ar being $-C(O)-O-C_{1-6}alkyl$.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

To those skilled in the chemical art, esters were held unpatentable over the prior art free acid because the idea of modifying carboxyl groups of compounds isomeric to the claimed compound was taught in another reference and no unusual utility inherent in the claimed esters was shown. *Ex parte Bergel et al.* (POBA 1949) 121 USPQ 522; *In re Ward* (CCPA 1964) 329 F2d 1021, 141 USPQ 227.

6. *Claim Rejections - Obvious Double Patenting*

Claims 2, 11-18, 20-22, and 25-26 are rejected under the judicially created doctrine obviousness-type double patenting as being unpatentable over claims 1-24 of Li et al. of US 2003/0096829. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current invention claims are embraced by the invention claimed in the above patent.

Determination of the scope and content of the prior art (MPEP §2141.01)

Li et al. disclosed a compound of formula (I) in claim 1, page 53 useful for treatment of asthma and inflammation.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims compounds and the prior art compounds is that the compounds of the instant claims has Y as a substituent in Ar being –COOH or $-C_{1-6}alkyl(C_{1-4}alkyl)_n$-COOH, wherein in the prior art the substituent in Ar being $-C(O)-O-C_{1-6}alkyl$.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

The instant claims 2, 11-18, 20-22, and 25-26 are therefore fully embraced by the prior art claims 1-24 because of the reason stated above in paragraph 5.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, In re Thorington, 418 F.2d 528, 168 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application

or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b).

Effective January 1,1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas Mckenzie, can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI
01/23/2007

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